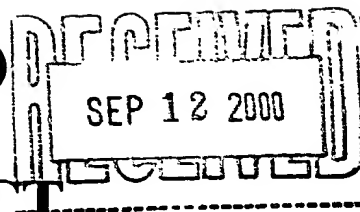


# PATENT COOPERATION TREATY



From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: JANE MASSEY LICATA  
LAW OFFICES OF JANE MASSEY LICATA  
66 E. MAIN STREET  
MARLTON, NJ 08053

**PCT**

## WRITTEN OPINION

(PCT Rule 66)

Docket System ☒  
Status Report ☒  
Docket Book ☒  
11/8/00 ANS

Date of Mailing (day/month/year) **08 SEP 2000**

Applicant's or agent's file reference

DRE-0019

**REPLY DUE**

within **TWO** months  
from the above date of mailing

International application No.

PCT/US99/28403

International filing date (day/month/year)

30 NOVEMBER 1999

Priority date (day/month/year)

30 NOVEMBER 1998

International Patent Classification (IPC) or both national classification and IPC

IPC(7): C12Q 1/70; C12P 19/34; C07H 21/04; C12N 5/00 and US Cl.: 435/6, 91.1, 372; 536/23.1

Applicant

DREXEL UNIVERSITY

1. This written opinion is the first (first, etc.) drawn by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

3. The applicant is hereby invited to reply to this opinion.

**When?** See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).~~

**How?** By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

**Also** For an additional opportunity to submit amendments, see Rule 66.4.  
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 *bis*.  
For an informal communication with the examiner, see Rule 66.6.

**If no reply is filed**, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 30 MARCH 2001

Name and mailing address of the IPEA/US

Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

BJ FORMAN

Telephone No. (703) 308-0196

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: JANE MASSEY LICATA  
LAW OFFICES OF JANE MASSEY LICATA  
66 E. MAIN STREET  
MARLTON, NJ 08053

## PCT

WRITTEN OPINION

(PCT Rule 66)

Date of Mailing (day/month/year) <span style="float: right; font-size: 1.2em;">08 SEP 2000</span>	
Applicant's or agent's file reference  DRE-0019	REPLY DUE within TWO months from the above date of mailing
International application No.  PCT/US99/28403	International filing date (day/month/year)  30 NOVEMBER 1999
Priority date (day/month/year)  30 NOVEMBER 1998	
International Patent Classification (IPC) or both national classification and IPC IPC(7): C12Q 1/70; C12P 19/34; C07H 21/04; C12N 5/00 and US Cl.: 435/6, 91.1, 372; 536/23.1	
Applicant DREXEL UNIVERSITY	

1. This written opinion is the first (first, etc.) drawn by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

3. The applicant is hereby invited to reply to this opinion.

**When?** See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).~~

**How?** By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

**Also** For an additional opportunity to submit amendments, see Rule 66.4.  
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 *bis*.  
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 30 MARCH 2001

Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer BJ FORMAN
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

## WRITTEN OPINION

International application No.

PCT/US99/28403

**I. Basis of the opinion****1. With regard to the elements of the international application:\***☒ the international application as originally filed☒ the description:

pages 1-13 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

☒ the claims:

pages 14 , as originally filed  
pages NONE , as amended (together with any statement) under Article 19  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

☒ the drawings:

pages NONE , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

☒ the sequence listing part of the description:

pages 1-3 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

**2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.**

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

**3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:**

- ☒ contained in the international application in printed form.  
☒ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

**4. ☒ The amendments have resulted in the cancellation of:**

- ☒ the description, pages NONE  
☒ the claims, Nos. NONE  
☒ the drawings, sheets/fig NONE

**5. ☐ This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".

WRITTEN OPINION

International application No.

PCT/US99/28403

**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. statement

Novelty (N)	Claims	<u>1-4</u>	YES
	Claims	<u>NONE</u>	NO
Inventive Step (IS)	Claims	<u>NONE</u>	YES
	Claims	<u>1-4</u>	NO
Industrial Applicability (IA)	Claims	<u>1-4</u>	YES
	Claims	<u>NONE</u>	NO

2. citations and explanations

Claims 1-4 lack an inventive step under PCT Article 33(3) as being obvious over Hoffmann-La Roche AG (N-Geneseq; ID No. Q10956) and Synergen Inc. (N-Geneseq; ID No. Q10907) in view of Duff et al.. The claims are drawn to a method and a kit for identifying individuals at risk of developing osteoporosis comprising assessing the genotype of tumor necrosis factor alpha 2 receptor gene and specific detection of a polymorphism at nucleotide positions 593, 598, and 620 in exon 10 of tumor necrosis factor alpha 2 receptor. Hoffmann-La Roche AG teach the claimed sequence of the tumor necrosis factor alpha 2 receptor and Synergen Inc. teach the claimed polymorphism in the tumor necrosis factor sequence. The claimed invention is obvious over Hoffmann-La Roche AG and Synergen Inc. in view of the teaching of Duff et al. who teach the tumor necrosis factor involvement in bone remodeling (Column 3, lines 21-24 and Column 4, lines 48-53). It would have been obvious to one skilled in the art to apply the teaching of Duff et al. to the sequences taught by Hoffmann-La Roche AG and Synergen Inc. for the obvious benefit of detecting specific sequences involved with osteoporosis.

Claims 1-4 meet the criteria set out in PCT Article 33(4), because the claimed method has clinical and commercial applications.

----- NEW CITATIONS -----

NONE

WRITTEN OPINION

International application No.

PCT/US99/28403

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**TIME LIMIT:**

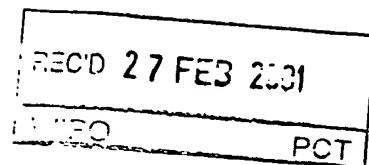
The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference <b>DRE-0019</b>	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. <b>PCT/US99/28403</b>	International filing date (day/month/year) <b>30 NOVEMBER 1999</b>	Priority date (day/month/year) <b>30 NOVEMBER 1998</b>
International Patent Classification (IPC) or national classification and IPC IPC(7): C12Q 1/70; C12P 19/34; C07H 21/04; C12N 5/00 and US Cl.: 435/6, 91.1, 372; 536/23.1		
Applicant <b>DREXEL UNIVERSITY</b>		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand <b>07 JUNE 2000</b>	Date of completion of this report <b>11 DECEMBER 2000</b>
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer <b>TERRY J. DEY</b> <b>PARALEGAL SPECIALIST</b> <b>TECHNOLOGY CENTER 1600</b> BJ FORMAN Telephone No. (703) 308-0196

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/28403

## I. Basis of the report

## 1. With regard to the elements of the international application: \*

- ☒ the international application as originally filed
- ☒ the description:  
pages 1-13, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the claims:  
pages 14, as originally filed  
pages NONE, as amended (together with any statement) under Article 19  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the drawings:  
pages NONE, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the sequence listing part of the description:  
pages 1-3, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_

## 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

## 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in printed form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE
- ☒ the claims Nos. NONE
- ☒ the drawings, sheets/fig NONE

5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/28403

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. statement**

Novelty (N)	Claims <u>1-4</u>	YES
	Claims <u>NONE</u>	NO
Inventive Step (S)	Claims <u>1-4</u>	YES
	Claims <u>NONE</u>	NO
Industrial Applicability (IA)	Claims <u>1-4</u>	YES
	Claims <u>NONE</u>	NO

**2. citations and explanations (Rule 70.7)**

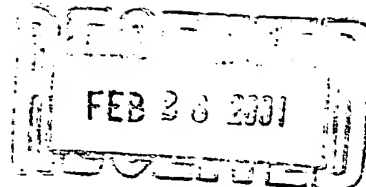
Claims 1-4 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the claimed methods and kits for identifying individuals at risk of developing osteoporosis. Specifically, the claims are drawn to methods and kits for identifying individuals at risk of developing osteoporosis comprising assessing the genotype of tumor necrosis factor alpha 2 receptor gene in a sample from the individual wherein the genotype comprising a polymorphism at nucleotides 593, 598, and 620 in exon 10 of the gene is indicative of the individual being at risk for developing osteoporosis. Hoffman-LaRoche AG (Geneseq; ID No. Q10956) teach the tumor necrosis factor alpha 2 receptor gene comprising a polymorphism at nucleotides 598 and 620 and Synergen Inc. (N-Geneseq; ID No. Q10907) teach the gene comprising a polymorphism at nucleotides 593 and 598. Additionally, Duff et al. (U.S. Patent No. 5,698,399) teach the tumor necrosis factor is involved in bone remodeling (Column 4, lines 48-53) and they teach methods for identifying individuals at risk of osteoporosis by identifying a polymorphism in the IL-1 gene (Column s 4-5). However, the prior art of record does not teach or suggest using the polymorphisms taught by Hoffman-LaRoche AG and Synergen, Inc. in the method of Duff et al. to obtain the claimed methods and kits for identifying individuals at risk of developing osteoporosis.

Claims 1-4 meet the criteria set out in PCT Article 33(4), because the claimed method has clinical and commercial applications.

----- NEW CITATIONS -----  
NONE



# PATENT COOPERATION TREATY



From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: JANE MASSEY LICATA  
LAW OFFICES OF JANE MASSEY LICATA  
66 E. MAIN STREET  
MARLTON, NJ 08053

Docket System ☒  
Status Report ☒  
Docket Book ☒

NP = 5/30/01

**PCT**

## NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing  
(day/month/year)

**22 FEB 2001**

Applicant's or agent's file reference

**DRE-0019**

### IMPORTANT NOTIFICATION

International application No.

**PCT/US99/28403**

International filing date (day/month/year)

**30 NOVEMBER 1999**

Priority Date (day/month/year)

**30 NOVEMBER 1998**

Applicant

**DREXEL UNIVERSITY**

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

#### 4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20531

Facsimile No. (703) 308-2330

Authorized officer

**BJ FORMAN**

Telephone No. (703) 308-0196

**TERRY J. DEY**  
**PARALEGAL SPECIALIST**  
**TECHNOLOGY CENTER 1600**

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>DRE-0019</b>	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. <b>PCT/US99/28403</b>	International filing date ( <i>day/month/year</i> ) <b>30 NOVEMBER 1999</b>	Priority date ( <i>day/month/year</i> ) <b>30 NOVEMBER 1998</b>
International Patent Classification (IPC) or national classification and IPC IPC(7): C12Q 1/70; C12P 19/34; C07H 21/04; C12N 5/00 and US Cl.: 435/6, 91.1, 372; 536/23.1		
Applicant <b>DREXEL UNIVERSITY</b>		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>3</u> sheets.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>0</u> sheets.</p> <p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I <input checked="" type="checkbox"/> Basis of the report</li> <li>II <input type="checkbox"/> Priority</li> <li>III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step or industrial applicability</li> <li>IV <input type="checkbox"/> Lack of unity of invention</li> <li>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI <input type="checkbox"/> Certain documents cited</li> <li>VII <input type="checkbox"/> Certain defects in the international application</li> <li>VIII <input type="checkbox"/> Certain observations on the international application</li> </ul>
--

Date of submission of the demand  <b>07 JUNE 2000</b>	Date of completion of this report  <b>11 DECEMBER 2000</b>
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer  <b>BJ FORMAN</b>
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

**TERRY J. DEY**

**PARALEGAL SPECIALIST**

**TECHNOLOGY CENTER 1600**

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/28403

## I. Basis of the report

## 1. With regard to the elements of the international application:\*

☒ the international application as originally filed☒ the description:

pages 1-13

pages NONE

pages NONE

, as originally filed  
, filed with the demand  
, filed with the letter of☒ the claims:

pages 14

pages NONE

pages NONE

pages NONE

, as originally filed  
, as amended (together with any statement) under Article 19  
, filed with the demand  
, filed with the letter of☒ the drawings:

pages NONE

pages NONE

pages NONE

, as originally filed  
, filed with the demand  
, filed with the letter of☒ the sequence listing part of the description:

pages 1-3

pages NONE

pages NONE

, as originally filed  
, filed with the demand  
, filed with the letter of

## 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).☐ the language of publication of the international application (under Rule 48.3(b)).☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

## 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☒ contained in the international application in printed form.☒ filed together with the international application in computer readable form.☐ furnished subsequently to this Authority in written form.☐ furnished subsequently to this Authority in computer readable form.☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4. ☒ The amendments have resulted in the cancellation of:☒ the description, pages NONE☒ the claims Nos. NONE☒ the drawings, sheets/fig NONE5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/28403

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. statement**

Novelty (N)

Claims 1-4 YESClaims NONE NO

Inventive Step (IS)

Claims 1-4 YESClaims NONE NO

Industrial Applicability (IA)

Claims 1-4 YESClaims NONE NO**2. citations and explanations (Rule 70.7)**

Claims 1-4 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the claimed methods and kits for identifying individuals at risk of developing osteoporosis. Specifically, the claims are drawn to methods and kits for identifying individuals at risk of developing osteoporosis comprising assessing the genotype of tumor necrosis factor alpha 2 receptor gene in a sample from the individual wherein the genotype comprising a polymorphism at nucleotides 593, 598, and 620 in exon 10 of the gene is indicative of the individual being at risk for developing osteoporosis. Hoffman-LaRoche AG (Geneseq; ID No. Q10956) teach the tumor necrosis factor alpha 2 receptor gene comprising a polymorphism at nucleotides 598 and 620 and Synergen Inc. (N-Geneseq; ID No. Q10907) teach the gene comprising a polymorphism at nucleotides 593 and 598. Additionally, Duff et al. (U.S. Patent No. 5,698,399) teach the tumor necrosis factor is involved in bone remodeling (Column 4, lines 48-53) and they teach methods for identifying individuals at risk of osteoporosis by identifying a polymorphism in the IL-1 gene (Column s 4-5). However, the prior art of record does not teach or suggest using the polymorphisms taught by Hoffman-LaRouch AG and Synergen, Inc. in the method of Duff et al. to obtain the claimed methods and kits for identifying individuals at risk of developing osteoporosis.

Claims 1-4 meet the criteria set out in PCT Article 33(4), because the claimed method has clinical and commercial applications.

----- NEW CITATIONS -----

NONE

## PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C.20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

<b>Date of mailing (day/month/year)</b> 11 September 2000 (11.09.00)	
<b>International application No.</b> PCT/US99/28403	<b>Applicant's or agent's file reference</b> DRE-0019
<b>International filing date (day/month/year)</b> 30 November 1999 (30.11.99)	<b>Priority date (day/month/year)</b> 30 November 1998 (30.11.98)
<b>Applicant</b> SPOTILA, Loretta, D.	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
07 June 2000 (07.06.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Manu Berrod

Telephone No.: (41-22) 338.83.38